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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,846	07/10/2001	Margaret O'Brien	55043	8176

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	16

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,846	O'BRIEN ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *16,18-23,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-15,17 and 24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Action is in response to the communication filed on 12/2/02, as Paper No. 15. In response to the restriction set forth in Paper No. 14 (mailed 9/23/02), Applicants elected Group I. However, upon further consideration the methods of elected Group I (methods for diagnosing susceptibility to normal/abnormal pregnancy, etc) are considered distinct methods and encompass analyzing distinct HLA-G polymorphisms. Therefore, the methods of Group I require further restriction and election of one of the Groups set forth below is required in any response to this action.

Applicant's election with traverse of Group I in Paper No. 15 (filed 12/02/2002) is acknowledged. The traversal is on the ground(s) that 1) Applicants disclosure that the combination of alleles in the mother and fetus play a role in determining whether the pregnancy is normal or abnormal, 2) the claims do not recite HLA-G per se and 3) a lack of unity was not set forth in the international stage of the application. This is not found persuasive because 1) It is acknowledge that the specification indicates that the combination of alleles in the mother and fetus play a role in determining whether the pregnancy is normal or abnormal, however, the claims are not so limited and can read on only identifying the HLA-G allele of one of the parents or of the fetus, because of the use of "and/or" in the claims, 2) Claim 18 is specifically drawn to a pharmaceutical composition comprising HLA-G, thus the claims do specifically recite HLA-G and 3) the result of the international stage of the application are non-binding, therefore it is appropriate to impose a restriction if proper. For the reasons set forth in the previous Action and below, the restriction is appropriate.

Claims 1-26 are pending in the application. Claims 16, 18-23, 25 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 15. Claims 1-15, 17 and 24 are addressed herein.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

As mentioned above, upon further consideration the methods of elected Group I (methods for diagnosing susceptibility to normal/abnormal pregnancy, etc) are considered distinct methods and encompass analyzing distinct HLA-G polymorphisms. Therefore, the methods of Group I require further restriction and election of one of the Groups set forth below is required in any response to this action.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s): 1 (steps: a, b and h only), 2, 4, 6, 7, 14 and 24 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by determining the sequence of an HLA-G nucleic acid.

Group II, claim(s): 1 (steps: a, c and h only), 6, 8, 10 (step f only), 11, 12, 13 and 14 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by detecting variant forms of HLA-G polypeptide.

Group III, claim(s): 1 (steps: a, d and h only), 3, 6, 8, 10 (step: a only), 11, 12, and 14 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by measuring the activity of HLA-G polypeptide.

Group IV, claim(s): 1 (steps: a, e and h only), 2, 3, 4, 6, 7, 10 (steps b and f only) 14 and 24 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by determining the size /level of HLA-G mRNA.

Group V, claim(s): 1 (steps: a, f and h only), 3, 6, 8, 10 (steps: b and f only), 11, 12, 13 and 14 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by determining the size/level of HLA-G polypeptide.

Group VI, claim(s): 1 (steps: a, g and h only), 6, 8, 9, 10 (step a only) 11, 12, 14 and 15 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by quantifying cells whose concentration changes as a result of HLA-G action.

Group VII, claim(s): 1 (steps: a, g and h only), 6, 8, 9, 10 (step a only) 11, 12, 14 and 15 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by quantifying molecules whose concentration changes as a result of HLA-G action.

Group VIII, claim(s): 1 (step a only), 5 (which depends only on claim 1 step a), 6, and 14 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by comparing variants by performing association and/or linkage analysis and/or transmission analysis.

Group IX, claim(s): 1 (step a only), 10 (steps c and d only, which depend only on claim 1 step a) and 17 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by measuring peptide binding of HLA-G.

Group X, claim(s): 1 (step a only), 10 (steps e only, which depend only on claim 1 step a) and 14 drawn to methods for diagnosing susceptibility to normal/abnormal pregnancy by measuring one or more molecules whose level is altered as a result of HLA-G (and HLA-G variants) and/or cells expressing HLA-G (and HLA-G variants) with blood mononuclear cells.

1. The inventions listed as Groups I-X above (and I-VII in the previous Office Action) do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The inventions are linked by HLA-G (the technical feature). However, there is no special technical feature linking the claims because in order for a technical feature to be "special" it must be novel. HLA-G was known in the prior art, as evidenced by Lee et al. (see Immunity Vol. 3:591-600; 1995, cited in the application on page 3 lines 12-20, and page 44, line 13). Therefore, the technical feature is not novel and there is no special technical feature linking the claims.

It is noted that claim 2 reads on three different polymorphisms of HLA-G, specifically, claim 2 reads on:

1) An HLA-G polymorphism having a C/T polymorphism of codon 93 in exon 3
2) An HLA-G polymorphism having a deletion of exon 8
3) An HLA-G polymorphism having a both a C/T polymorphism of codon 93 in

exon 3 and a deletion of exon 8.

These polymorphisms constitute patentably distinct HLA-G polymorphisms because each polymorphism is structurally distinct (has a unique sequence) and because each HLA-G polymorphism has a different function resulting in different effects, such as an increase in the risk of pre-ecamplasia. For instance, a normal HLA-G would not indicate a risk to pre-ecamplasia while the HLA-G polymorphism of exon 3 would indicate a risk to ecamplasia, the HLA-G polymorphism of exon 8 would indicate a different level of risk to ecamplasia, and the HLA-G polymorphism of both exons 3 and 8 would indicate a greater risk to ecamplasia than the exon 3 or 8 polymorphism alone. Therefore, the methods related to the different polymorphisms are different methods and restriction to a single invention (i.e. a single polymorphism) is appropriate. In response election of the one of the polymorphisms is required (if a corresponding SEQ ID NO corresponds to the elected polymorphism (e.g. possibly SEQ ID NO: 16-19 or the polypeptide encoded by SEQ ID NO: 16-19) then identification of the corresponding SEQ ID NO is required as well.

It is noted that claim 24 reads on using different sequences for diagnosing susceptibility to normal/abnormal pregnancy as well as using the different sequences in a kit, monitoring progress of pregnancy, manufacturing medicament, screening methods, improving pregnancy, preventing disorders and monitoring the progress of pregnancy. Claim 24 will only be examined to the extent that it reads on the elected invention.

Furthermore, the exact sequences which are to be used in the diagnostic method need to be identified. For instance, the SEQ ID NO corresponding to the exact HLA-G polymorphism needs to identified as well as the exact sequence primers which can be used to specifically identify the elected polymorphism.

Therefore, a proper response will contain an election of one of the above groups as well as the specific HLA-G nucleic acid or polypeptide. If groups 1 or 4 are elected then the exact sequence primers used to sequence or measure the size/level of the HLA-G mRNA also needs to be elected.

2. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVE T. NGUYEN
PRIMARY EXAMINER

J. Eric Angell
February 10, 2003